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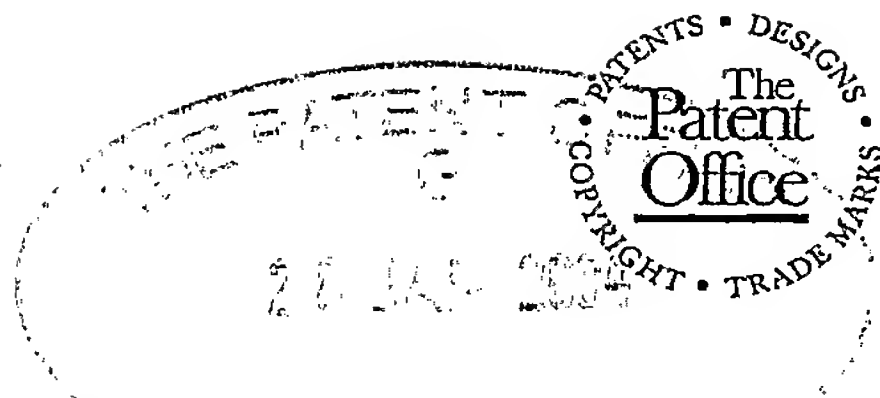
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1. Your reference N90485 JEB

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3. Full name, address and postcode of the or of each applicant (underline all surnames)  
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Patents ADP number (if you know it) 8147845001

If the applicant is a corporate body, give the country/state of its incorporation

4. Title of the invention Novel Particles

5. Name of your agent (if you have one) J. A. KEMP & CO.

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Patents ADP number (if you know it) 26001

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Description	7
Claim(s)	2
Abstract	1
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Statement of inventorship and right to grant of a patent (Patents Form 7/77)

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Signature(s)

J.A. KEMP & CO.

Date 28 January 2004

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J E BENSON  
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## NOVEL PARTICLES

The present invention relates to novel particles which find utility as degradation protectors, for example in UV screening compositions suitable for cosmetic and topical pharmaceutical use.

5        In our British Application No. 0315082.8 we describe how the degradation of organic sunscreen agents, and other components which are susceptible to degradation, can be retarded if the compositions also have present zinc oxide or titanium dioxide which has been doped with another element and/or reduced zinc oxide. These can be regarded as degradation protectors because they help to protect  
10    sunscreen ingredients which are unstable to sunlight against sunlight-induced photo-degradation. By using these doped or reduced materials rather than ordinary titanium dioxide or zinc oxide it is, for example, possible either to provide a composition which gives better protection against UV light for the same quantity of organic sunscreen agent or a composition having the same screening effect against UV light  
15    but containing a smaller quantity of organic sunscreen agent.

      In our co-pending British Patent Application, filed on the same day as this application and entitled Degradation Protectors, we describe how it is important that if the oxide is to be really effective there must be dopant on a surface thereof which can interact with the component of the composition to be protected. For example if,  
20    in a two phase composition, the oxide is present in the aqueous phase and the component to be protected is in the organic phase there is little interaction because of the phase boundary. Thus the free radicals generated by degradation of the component cannot contact the dopant without moving from one phase to another. It has further been realised that if the dopant is solely in the bulk it is not able to  
25    interact effectively (as a free radical scavenger) with the component of the composition to be protected. A consequence of this is that it is possible to use materials which are only surface doped, i.e. where there is dopant in or on the surface of the particle. Such particles are believed to be novel and these form the subject of the present invention.

30        Accordingly the present invention provides a particle of  $\text{TiO}_2$  or  $\text{ZnO}$  which has been doped with one or more other elements such that the concentration of

dopant in a surface of the particle is greater than that at a core of the particle.

The expression "in the surface", as used herein, means, assuming a substantially spherical particle, the outer shell which has a thickness not exceeding 10% of the radius of the particle. It will be appreciated that the presence of dopant  
5 "in the surface" which includes "at the surface" is to be contrasted with material which can be on the surface as in the case of a simple coating. "At the surface" means dopant which is bound to the particle other than by pure electrostatic forces as is the case with a coating. As used herein, the term "the core" means, assuming a substantial spherical particle, the sphere at the centre of the particle whose radius  
10 does not exceed 10% of the radius of the particle (or, in the case of substantially non-spherical particles, 10% of the largest dimension). The term "bulk of the particle" means the particle excluding the said outer shell.

It is preferred that the concentration of dopant in the surface of the particle is greater than that in the bulk of the particle and it is particularly preferred that there is  
15 no dopant at the core of the particle. In other words, there will be a concentration gradient e.g. such that the ratio of dopant atoms to titanium or zinc atoms in the surface is greater than the ratio in the core or centre where it may be zero.

The optimum total amount of the second component on the particle may be determined by routine experimentation, but it is preferably low enough so that the  
20 particles are minimally coloured. Amounts as low as 0.1 mole % or less, for example 0.05 mole %, or as high as 1 mole % or above, for example 5 mole % or 10 mole %, can generally be used. Typical concentrations are from 0.5 to 2 mole % by weight. The mole ratio of dopant to host metal on the surface is typically from 2-25:98-75, usually 5-20:95-80 and especially 8-15:92-85. The amount of dopant at the surface  
25 can be determined by, for example, X-ray Photoelectron Spectroscopy (XPS).

Suitable dopants for the oxide particles include manganese, which is especially preferred, e.g.  $\text{Mn}^{2+}$  but especially  $\text{Mn}^{3+}$ , vanadium, for example  $\text{V}^{3+}$  or  $\text{V}^{5+}$ , chromium, cerium, selenium and iron but other metals which can be used include nickel, copper, tin, e.g.  $\text{Sn}^{4+}$ , aluminium, lead, silver, zirconium, zinc, cobalt, e.g.  
30  $\text{Co}^{27}$ , gallium, niobium, for example  $\text{Nb}^{5+}$ , antimony, for example  $\text{Sb}^{3+}$ , tantalum, for example  $\text{Ta}^{5+}$ , strontium, calcium, magnesium, barium, molybdenum, for example

Mo<sup>3+</sup>, Mo<sup>5+</sup> or Mo<sup>6+</sup> as well as silicon. These metals can be incorporated singly or in combinations of two or three or more. It will be appreciated that for effective bulk doping the size of the ion must be such as can readily be inserted into the crystal lattice of the particle. On the other hand there is no such size limitation for the  
5 elements used in surface doping; preferred surface dopants include manganese, eg. as Mn<sup>2+</sup>, cerium, selenium, iron, chromium and vanadium.

The surface-doped particles of the present invention can be obtained by any one of the standard processes for preparing such doped oxides and salts. Titanium oxide and zinc oxide are generally doped by two basic methods involving either  
10 coprecipitation or absorption, although other processes including flame pyrolysis can be used provided there is sufficient dopant at the surface. It will be appreciated that coprecipitation will generally result in a fairly uniform distribution of dopant throughout the particle with a result that such procedures are generally not suitable for preparing the particles of the present invention. On the other hand, absorption  
15 processes can readily be used provided that the process is stopped before the dopant becomes absorbed substantially uniformly to the core. In other words, if the procedure is stopped at a stage earlier than one would normally use to obtain doped material then one can obtain particles where the concentration of dopant is greater in the surface than at the core.

20 This can be achieved by using, for example, shorter reaction times. It will be appreciated that the dopant need not necessarily be present as an oxide but may be present as a salt such as a chloride or salt with an oxygen-containing anion such as perchlorate or nitrate. Such techniques include a baking technique by combining particles of a host lattice (TiO<sub>2</sub>/ZnO) with a second component in the form of a salt  
25 such as a chloride or an oxygen-containing anion such as a perchlorate or a nitrate, in solution or suspension, typically in solution in water, and then baking it, typically at a temperature of at least 300°C and then calcining it at a higher temperature, for example at least 500° or 600°C. Accordingly the present invention provides a process for preparing the particles of the present invention which comprises placing a particle  
30 of TiO<sub>2</sub> or ZnO in contact with a solution or suspension of a salt of the dopant for a

time insufficient for the concentration of dopant salt in the core of the particle to reach that at its surface and then baking the resulting particle.

It will be appreciated that such baking techniques and the like will result in dopant in the surface forming part of the crystal lattice while in coating the dopant will remain as a separate layer on the particle surface. It may well be the case that if the dopant is to quench internally generated free radicals effectively then it needs to be in the crystal lattice.

The rutile form of titania is known to be less photoactive than the anatase form and is therefore preferred.

10 The zinc oxide subjected to surface doping can be reduced zinc oxide. Reduced zinc oxide particles (i.e. particles which possess an excess of zinc ions relative to the oxygen ions) may be readily obtained by heating zinc oxide particles in a reducing atmosphere to obtain reduced zinc oxide particles which absorb UV light, especially UV light having a wavelength below 390 nm, and re-emit in the green, 15 preferably at about 500 nm. Typically the concentration of hydrogen is from 1 to 20%, especially 5 to 15%, by volume, with the balance inert gas, especially nitrogen. A preferred reducing atmosphere is about 10% hydrogen and about 90% nitrogen by volume. The zinc oxide is heated in this atmosphere at, say, 500° to 1000° C, generally 750 to 850° C, for example about 800° C, for 5 to 60 minutes, generally 10 20 to 30 minutes. Typically it is heated to about 800° C for about 20 minutes. It will be understood that the reduced zinc oxide particles will contain reduced zinc oxide consistent with minimising migration to the surface of the particles of electrons and/or positively charged holes such that when said particles are exposed to UV light in an aqueous environment the production of hydroxyl radicals is substantially 25 reduced as discussed above.

It is believed that the reduced zinc oxide particles possess an excess of  $\text{Zn}^{2+}$  ions within the absorbing core. These are localised states and as such may exist within the band gap. A further discussion of this can be found in WO 99/60994.

The average primary particle size of the particles is generally from about 1 to 30 200 nm, for example about 1 to 150 nm, preferably from about 1 to 100 nm, more

preferably from about 1 to 50 nm and most preferably from about 20 to 50 nm. The particle size is preferably chosen to prevent the final product from appearing coloured. Thus nanoparticles are frequently used. Since the scavenging effect is believed to be essentially catalytic it is desirable that the particles are as small as possible to maximise their surface area and hence the area of doped material on the surface. This small size has the advantage that less dopant is needed which has the consequential advantage that any colouring effect caused by the dopant is reduced. However, in one embodiment slightly larger particles for example from 100 to 500 nm, typically 100 to 400 or 450 nm especially from 150 to 300 nm and particularly 200 to 250 nm, can be employed. These provide good coverage of, for example, skin imperfections without unacceptable skin whitening.

Where particles are substantially spherical then particle size will be taken to represent the diameter. However, the invention also encompasses particles which are non-spherical and in such cases the particle size refers to the largest dimension.

The oxide particles of the present invention may have an inorganic or organic coating. For example, the particles may be coated with oxides of elements such as aluminium, zirconium or silicon, especially silica or, for example, aluminium silicate. The particles of metal oxide may also be coated with one or more organic materials such as polyols, amines, alkanolamines, polymeric organic silicon compounds, for example,  $\text{RSi}[\{\text{OSi}(\text{Me})_2\}_x\text{OR}^1]_3$  where R is  $\text{C}_1\text{-C}_{10}$  alkyl,  $\text{R}^1$  is methyl or ethyl and x is an integer of from 4 to 12, hydrophilic polymers such as polyacrylamide, polyacrylic acid, carboxymethyl cellulose and xanthan gum or surfactants such as, for example, TOPO. If desired the surface doping can be carried out by a coating technique either separately or in combination with the inorganic or organic coating agent. Thus for example the undoped oxide can be coated with, say, manganese oxide along with an organic or inorganic coating agent such as silica. It is generally unnecessary to coat the oxide particles to render them hydrophilic, so that for the aqueous phase the particles can be uncoated. However if the particles are to be in the organic or oily phase their surface needs to be rendered hydrophobic or oil-dispersible. This can be achieved by the application directly of, for example, a suitable hydrophobic polymer or indirectly by the application of a coating, for

example of an oxide such as silica (which imparts a hydrophilic property) to which a hydrophobic molecule such as a metal soap or long chain (e.g.  $C_{12} - C_{22}$ ) carboxylic acid or a metal salt thereof such as stearic acid, a stearate, specifically aluminium stearate, aluminium laurate and zinc stearate.

- 5        It should be understood that the term "coating" is not to be construed as being limited to a complete covering. Indeed it is generally beneficial for the coating not to be complete since the coating can act as a barrier to the interaction of the free radicals with the dopant on or in the surface of the particle. Thus it is preferred that the coating should be discontinuous where maximum scavenging effect is desired.
- 10       However it will be appreciated that dopant on the surface can still act to quench free radicals generated within the particle in which case the coating can be continuous.. Since coatings of silanes and silicones which can be polymeric or short chain or monomeric silanes are generally continuous these are generally less preferred. Thus coating with an inorganic oxide is generally preferred since these generally do not
- 15       result in a complete coating on the surface of the particles.

Typical coating procedures include the deposition of silica by mixing alkali such as ammonium hydroxide with an orthosilicate, such as tetraethylorthosilicate, in the presence of the particle. Alternatively the particle can first be coated with a silane such as (3-mercaptopropyl) trimethoxy silane (MPS) and then silicate e.g.

20       sodium silicate is added. The silane attaches to the particle surface and acts as a substrate for the silicate which then polymerises to form silica. Similar techniques can be used for other inorganic oxides.

The particles of the present invention can be used in all the compositions described in our co-pending British Patent Application referred to above, and they are

25       also useful in the polymer and agricultural compositions described in our further co-pending British Patent Applications also filed on the same day as this application and entitled Improved Polymeric Composition and Improved Agricultural Compositions.

The following Example further illustrates the present invention.

**Acid Extraction of Manganese Doped Titania**

30       Samples of manganese doped titania were soaked in 25% hydrochloric

acid for various times at room temperature. The titania was settled by centrifugation and the supernatant liquid transferred to a 50ml volumetric flask. The titania was washed once by re-suspension in water with the aid of ultrasonics and again centrifuged. The washings were added to the volumetric flask and the contents made  
5 to 50 ml. with de-ionised water.

Samples of the extracts, together with the original powder samples, were analysed for manganese. The water extracts were analysed directly by AAS (Atomic Absorption Spectroscopy). The powders were similarly analysed, after digestion with a hydrofluoric acid-sulphuric acid mixture.

10

**DPPH (Radical Scavenging) Assay.**

A stock solution of 1mM DPPH in MeOH was made. Samples containing 120 $\mu$ l of DPPH (1mM) plus 300 $\mu$ l TiO<sub>2</sub> (3 mg/ml) were made up to 3ml with MeOH and were placed in a 10 mm quartz cuvette. DPPH is a stable radical, which absorbs at 520nm, therefore a loss of absorbance at this wavelength, is a  
15 measure of the radical scavenging ability of the TiO<sub>2</sub>. The titania samples were taken from the above series of extractions. The samples were kept in the dark and the absorbance at 520 nm measured every 5 minutes. The samples required mixing before each measurement was taken in order to redisperse the TiO<sub>2</sub>.

20

Time of exposure (hrs)	Extracted Mn (%)	Rate of loss of DPPH (mAbs/min)
0	0	3.4
0.25	3.22	2.05
1.5	4.58	1.6
25 48	26.0	0.35

It is clear from these data that 74% of the manganese remained after 48 hours. As the rate of loss of DPPH is then very small it is clear that it is the remaining 26% of the manganese which is in or on the surface which acts to scavenge free radicals.  
30 Thus particles having manganese available at the surface will scavenge free radicals.

## CLAIMS

1. A particle of  $\text{TiO}_2$  or  $\text{ZnO}$  which has been doped with one or more other elements such that the concentration of dopant in a surface of the particle is greater than that at a core of the particle.
- 5 2. A particle according to claim 1 wherein the said concentration is greater than that in the bulk of the particle.
3. A particle according to claim 1 or 2 wherein there is no dopant at the core of the particle.
4. A particle according to any one of the preceding claims which is  
10 coated with a discontinuous layer of hydrophilic or hydrophobic material.
5. A particle according to claim 4 which is coated with a hydrophobic polymer.
6. A particle according to claim 4 which is coated first with an oxide of aluminum, zirconium or silicon and then with a long chain carboxylic acid salt.
- 15 7. A particle according to any one of the preceding claims wherein the dopant is manganese, vanadium, chromium, iron, selenium or cerium.
8. A particle according to claim 7 wherein the dopant is  $\text{Mn}^{2+}$ .
9. A particle according to claim 7 wherein the dopant is  $\text{V}^{4+}$ .
10. A particle according to any one of the preceding claims wherein the  
20 dopant is present in an amount from 0.5 to 2 mole % by weight.
11. A particle according to any one of the preceding claims which is doped titanium dioxide.
12. A particle according to any one of the preceding claims wherein the titanium dioxide is in rutile form.
- 25 13. A particle according to any one of the preceding claims which has a particle size from 1 to 200 nm.
14. A particle according to any one of claims 1 to 12 wherein the doped or reduced oxide has a particle size from 100 to 500 nm.
15. A particle according to any one of the preceding claims wherein the  
30 mole ratio of dopant to host metal at the surface is 2-25 to 98-75.

16. A particle according to claim 15 wherein the mole ratio of dopant to host metal at the surface is 8-75 to 92-25.

17. A particle according to claim 1 substantially as hereinbefore described.

5 18. A process for preparing a particle as claimed in any one of the preceding claims which comprises placing a particle of  $\text{TiO}_2$  or  $\text{ZnO}$  in contact with a solution or suspension of a salt of the dopant for a time insufficient for the concentration of dopant salt in the core of the particle to reach that at its surface and then baking the resulting particle.

10 19. A process according to claim 18 wherein the particle is baked at a temperature of at least  $500^\circ\text{C}$ .

20. A process according to claim 18 substantially as hereinbefore described.

15 21. A particle according to any one of claims 1 to 17 whenever prepared by a process as claimed in any one of claims 18 to 20.

### ABSTRACT

A particle of  $\text{TiO}_2$  or  $\text{ZnO}$  which has been doped with one or more other elements such that the concentration of dopant in the surface of the particle is greater  
5 than that at the core of the particle.